REMARKS

The Office action mailed August 11, 2006 has been received and reviewed. Claims 1-13 and 15-18 were pending. Claims 1-3 and 15-18 were rejected. The application is to be amended as previously set forth. All amendments and claim cancellations are made without prejudice or disclaimer. No new matter has been added. Reconsideration is respectfully requested.

A. Claim 15 and 35 U.S.C. § 112, first paragraph:

Claim 15 was rejected under 35 U.S.C. § 112, first paragraph, as assertedly lacking adequate written description. Applicants have amended claim 15, and in view of the amendment, respectfully request that the rejection be withdrawn.

Specifically, applicants have amended claim 15 to be directed to an isolated polynucleotide sequence selected from the group consisting of an isolated polynucleotide comprising a polynucleotide sequence of SEQ ID NO:1 and an isolated polynucleotide encoding the polypeptide sequence of SEQ ID NO:2, which should overcome the rejections.

New claim 19 somewhat parallels claim 15, but uses the means plus function format specifically sanctioned by 35 U.S.C. § 112, sixth paragraph. *See*, M.P.E.P., § 2181 *et seq*.

B. Claims 1-3 and 15-18 and 35 U.S.C. § 103:

Claims 1-3 and 15-18 were rejected under 35 U.S.C. § 103 as being obvious in view of Theodoulou and Dudler et al.

The rejection is based on the assumptions that it would have been obvious to take a plant ABC transporter gene encoding a protein having similar structural motifs to the human MRD ABC transporter and test it for inducing or enhancing production or secretion of an alkaloid such as taxol to determine the function of the plant MDR homologue. The motivation was asserted to be Theodoulou's alleged teaching that taxol and other plant secondary metabolites are substrates of or bind MDR ABC transporter proteins and would thus be useful in bioengineering secondary product production in plants or plant cells that produce taxol or other plant secondary compounds. Since transgenic strategies for evaluating the specific function of plant ABC transporter genes were within the reach of one of ordinary skill in the art and non-plant alkaloid transporters and methods of transforming plants and maintaining plant cell cultures for the

production of secondary metabolites were known in the art, one would allegedly have had a reasonable expectation of success.

Applicants respectfully traverse the rejection.

With regard to this analysis, it appears that this reading of portion 5.2 of Theodoulou (admittedly the most relevant portion) was done with impermissible hindsight. Indeed, the following is clearly stated in portion 5.2:

> "The first and, to date, only functional characterization of a plant P-gp was achieved with transgenic plants. . . . [These results] demonstrated the involvement of AtPGP1 in hypocotyl cell elongation in the light. The authors propose that AtPGP1 is involved in the export of a signal compound . . . . A plasma membrane location for AtPGP1 is also consistent with a signalling/export role.
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> Examination of the ABC transporter literature suggests a range of putative functions: for example, yeast STE 6 transport peptides, mammalian MDR2 functions as a phospholipid translocator, and P-gp/MDR1 exports cytotoxic drugs from the cells and acts as a channel regulator – all these are plausible functions for P-gp homologues in plants. Moreover, the fact that plant secondary products such as vincristine and taxol are often substrates for, or inhibitors of, MDR proteins suggests a role of plant P-gp in synthesis and compartmentation of these compounds. It is not possible to predict substrate based on primary structure/sequence homology: the products of even closely related genes can have markedly different functions and site-directed mutagenesis of many types of transport protein has shown that single amino acid changes can radically alter substrate specificity. . . ."

Theodoulou, p. 86 (citations omitted).

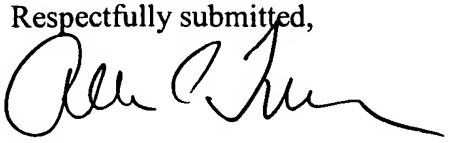
Based on Theodoulou, an ordinarily skilled person interested in secondary metabolite production in plants could at best discern that ABC transporters could serve several functions, *inter alia*, an export function and possibly serving a role in the synthesis of secondary metabolites (which could result either in an increased or decreased synthesis).

In contrast, applicants found that one can use ABC transporters to increase the amount of secondary metabolites produced (and thus the secondary metabolites' production or secretion). No single straightforward suggestion exists in Theodoulou motivating an ordinarily skilled person - without any doubt - to use ABC transporters to increase the yield of secondary metabolites, particularly without undue experimentation. At most, a skilled person might be

invited to try it via experimentation, but he or she would not have any reasonably expectation of success in that regard. Hence, applicants believe that the claimed invention is not obvious.

The application should now be in condition for allowance. If questions remain after consideration of the foregoing, the Office is kindly requested to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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